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# Possible predictors of Covid-19 vaccine hesitancy in the psychiatric population – A scoping review



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#### ABSTRACT

Background: The Covid-19 pandemic brought vaccination to the front of the series of measures implemented to address the chain-reaction outbreaks that continue to cause loss and suffering. In spite of its proven efficacy, a considerable percentage of the population remains hesitant or right-out opposed. A need for informing public health strategies not only in regards to the current pandemic but for future similar developments remains of utmost importance for researchers and clinicians alike, especially when it comes to vulnerable categories of population. Identifying risk factors associated with vaccine hesitancy in the psychiatric population is the aim of this scoping review.

Methods: We performed a systematic search on the topic of Covid-19 vaccine hesitancy in relation to psychiatric disorders, using three databases: Medline, PubMed and Embase. Inclusion criteria focused on studies looking at individuals with a psychiatric disorder in the context of the Covid-19 vaccine hesitancy where possible determinant factors were discussed.

*Results*: Fifteen articles out of 219 publications on the topic of Covid 19 vaccine hesitancy met our inclusion criteria for this review. The common findings of these studies recognize the following risk factors for Covid 19 hesitancy: diagnosis of severe mental illness such as schizophrenia, lower socioeconomic status, lower educational level, and young age.

Conclusions: Our findings may contribute to the proactive development of educational strategies targeting the psychiatric population in the context of cultural, ethnic, age and gender diversity, in order to safeguard the wellbeing of all when facing pandemic events. Overarching future directions include creating vaccination promotion strategies specific for the psychiatric population.

## 1. Introduction

Vaccination is one of the most important and effective tools used to prevent infectious diseases at population and/or individual levels (WHO, 2019). The Covid-19 pandemic, the most recent and profoundly impactful at a global level, brought this intervention to the front of the series of measures implemented to address the chain-reaction outbreaks that continue to cause loss and suffering. Mass-media controversies around its efficacy, adverse effects, and alleged behind-the-scene interests of political powers complicate the implementation of preventative measures, with a considerable percentage of the population still hesitant or right-out opposed. Defined as "delay in acceptance or refusal of vaccines despite availability of vaccination services" by the World Health

Organization (MacDonald, 2015), vaccine hesitancy has become a forefront player in the strategic pandemic response.

With most countries reporting a significant success rate in vaccination, the problematic sector evading it continues to present as a challenge, where the factors involved are yet to be clearly defined. The scientific community experienced an expected and necessary shift in priority studying pandemic-related problematics while scientific journals published a significant number of articles, comments, and perspectives on the topic. Patients with severe mental illness, it was identified, are more likely to suffer from severe clinical outcomes of COVID-19 than people without a mental illness (Wang et al., 2021).

A 2020 large-scale study of COVID-19 in UK health care workers from diverse ethnic backgrounds, using measures of vaccine hesitancy, found a

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series of predictors of greater vaccine hesitancy: lower pro-vaccination attitudes; no flu vaccination in 2019–2020; pregnancy; higher COVID-19 conspiracy beliefs; younger age; and lower optimism at the roll-out of population vaccination (MacManus et al., 2021). Considering the high prevalence of some of these contributing factors in the psychiatric population regardless of the pandemic situation, we set out to explore the literature for factors identified as possible predictors of vaccine hesitancy in this category of vulnerable individuals. A need for informing public health strategies not only in regards to the current pandemic but for future similar developments remains of utmost importance for researchers and clinicians alike and it is the aim of this scoping review to aid in this process.

#### 2. Methods

# 2.1. Search strategy and eligibility criteria

We performed a systematic search on the topic of Covid-19 vaccine hesitancy in relation to psychiatric disorders using three databases: Medline, PubMed, and Embase, on August 21, 2022. The terms of our search on Medline were: (Covid-19) AND (Mental Disorders) AND (Vaccination hesitancy OR vaccine hesitancy); on PubMed: ((Mental disorders) AND (Covid-19)) AND (vaccination hesitancy); on Embase: (mental disease OR mental illness) AND (Covid-19) AND (vaccination hesitancy). A total of 219 publications identified in these databases returned articles published over the two years of the pandemic with 19 from Medline, 28 from PubMed, and 172 from Embase. We included all

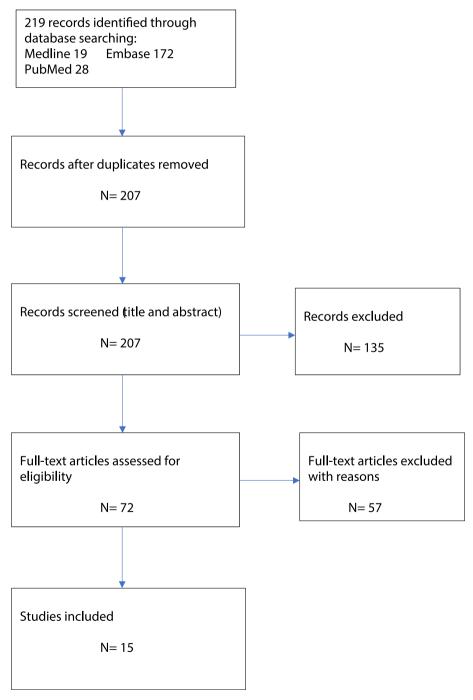


Fig. 1. Flow chart diagram of search strategy.

 Table 1

 Study population characteristics, outcome measures and main findings in the selected studies.

Study	Type of Study, Location and Characteristics	Outcome Measures and Main Findings (1. Pro-vaccination factors; 2. Vaccine hesitancy predictors; 3. Other findings.)
Eyllon et al. (2022)	$\label{eq:cross-sectional study} \\ Northeastern United States \ n = 14\ 365\ patients \ of \ a \ group \\ medical \ practice$	Outcome measures: online survey Main Findings:
		2. Substance and tobacco use disorders had vaccine hesitancy after regression analysis of sociodemographic factors; Medicaid payer type, lower education, income and Hispanic, female, and African American groups were associated with more vaccine hesitancy; younger respondents and those with lower socioeconomic status were more likely to report vaccination resistance.
		3. More vaccine hesitancy across all psychiatric comorbidities except Alcohol Use Disorders
Huang et al. (2021)	Cross-sectional study Wuhan, China N = 006 edult patients with mental disorders	Outcome measures: self-administered questionnaire Main findings:
	N=906 adult patients with mental disorders	<ol> <li>Higher education, a good family financial status, believing that over 50% of vaccine recipients would be immune to COVID-19, not being worried about side-effects, being out-patients, having mental disorders other than psychosis significantly associated with vaccine uptake</li> <li>2.psychotic disorders were least likely to take the vaccine</li> </ol>
Jefsen et al., 2021	Cross-sectional study $ Danish \ Population \ n=992 \ patients \ from \ psychiatric $	Outcome measures: questionnaire-based online surveys Main findings:
	services	<ol><li>Younger age and mental illness were associated with lower vaccination willingness; Reasons for vaccine hesitancy: safety concerns, vaccines not sufficiently tested, vaccination</li></ol>
Uvais (2021)	Cross-sectional study Indian population	unnecessary, lack of trust in authorities  Outcome measures: Covid-19 related questionnaire  Main findings:
	N=90 patients of an outpatient psychiatry department	<ol> <li>Patients with higher education had more intentions of vaccination;</li> <li>Islamic participants had significantly higher vaccine hesitancy;</li> <li>Significantly higher vaccine hesitancy in this population in comparison to other global</li> </ol>
Bai et al., 2021	Cross-sectional study Chinese Population $N=1853$ outpatients and inpatients associated with 6 psychiatric hospitals	populations.  Outcome measures: survey containing items from the WHO Quality of Life Scale Brief version (WHOQOL-BREF), the Visual Analog Scale for Pain (VAS), Patient Health Questionnaire-2 (PHQ-2), Social Impact Scale (SIS)  Main findings:
Perlis et al. (2022)	Cross-sectional study	Unemployed, severe mental illnesses, higher perceived vaccine stigma; living in community dwellings     Outcome measures: online survey
	American Population $N=15$ , 464 respondents of which 4164 identified depressive symptoms	Main findings:     Depression and endorsing misinformation     Diagnosis with depression was significantly associated with increased likelihood of endorsing misinformation after adjustment for sociodemographic features, ideology and political affiliation
Danenberg et al. (2021)	Cross-sectional study	Outcome measures: the Outcome Questionnaire-45 (OQ-45); Fear of Covid-19 (FCV–19S); Covid-19 Vaccine Hesitation Scale (C19-VHS)  Main findings:
Sullivan et al.,	psychiatric hospital  Cross-sectional study	<ol> <li>Anxiety (fear of Covid-19); higher education</li> <li>Lack of confidence in the need to be vaccinated, risk perception and fear of side effects</li> <li>Majority of patients who are suffering from severe mental illness are willing to get vaccinated</li> <li>Outcome measures: computer-assisted self-report on physician trust, Covid-19 vaccination</li> </ol>
2022	$\label{eq:normalized_normalized} \mbox{N} = 109 \mbox{ people with Opioid Use Disorder}$	willingness Main findings:
Hao et al. (2021)	Cross-sectional study Chongqing, China anxiety disorder $(n = 79)$ and healthy	<ol> <li>Trust in physician was positively associated, but not significantly correlated, with willingness to receive partially effective vaccine</li> <li>Black Americans were less likely to report willingness to use safe and partially effective vaccine         Outcome measures: Covid-19 related questionnaire; Depression, Anxiety and Stress Scale (DASS-21)</li> </ol>
True Pitan et el	controls ( $n = 134$ )	Main findings:  1. More people with depression/anxiety were found to be willing to pay >\$250 for vaccine
	Longitudinal Cohort Study	<ul> <li>(associated with high DASS-21 score)</li> <li>High proportion of vaccination willingness in depression/anxiety patients compared to other similar studies</li> <li>Outcome measures: datasets from database mining</li> </ul>
Tzur Bitan et al., 2021	Longitudinal Cohort Study Israel $N=51,078$ individuals with schizophrenia and controls (N	Outcome measures: datasets from database mining Main findings:
	= 25539 SZ N = 25 539 controls)	<ol> <li>Older age, being male, medium to high SES, being married, affiliated with general Jewish population, having obesity and hyperlipidemia</li> <li>Schizophrenia was negatively associated with vaccination</li> </ol>
		<ol><li>Schizophrenia patients had higher rates of obesity, smoking, diabetes, hyperlipidemia and COPD;</li></ol>

(continued on next page)

Table 1 (continued)

Study	Type of Study, Location and Characteristics	Outcome Measures and Main Findings (1. Pro-vaccination factors; 2. Vaccine hesitancy predictors; 3. Other findings.)
McNeil and Purdon, 2022	Cross-sectional study $N=96 \ individuals \ with \ an \ anxiety \ disorder \\ N=52 \ no \ anxiety \\ Recruited \ from \ the \ Anxiety \ Studies \ database \ University \ of \ Waterloo, \ Ontario$	Schizophrenia patients had sharper decline in survival rates and significantly sharper increase in probability of COVID-19 hospitalization and mortality rates as time passed.  Outcome measures: Vaccine hesitancy scale (VHS); COVID stress scale (CSS); Cultural cognition worldview scale individualism-communitarianism subscale (CCWS); Conspiratorial beliefs scale -generic; Hong's psychological reactance scale (HPRS); Intolerance of uncertainty Scale; Trust Scale; Disgust propensity and sensitivity scale.  Main findings:
Nishimi et al., 2022	$\label{eq:Longitudinal} \begin{tabular}{ll} Longitudinal online study \\ N=544~US~adults~with~high~levels~of~pre-pandemic~trauma~and~PTSD \end{tabular}$	<ol> <li>Top reasons to get the vaccine were to protect others and self.</li> <li>Intolerance of uncertainty was associated with greater hesitancy in those without anxiety; influenza vaccine history, conspiracy beliefs, individualism and trust concerns about adverse effects and efficacy;</li> <li>Outcome measures: Online survey on mental health and Covid-19 experiences; Trauma History Screen; PTSD Checklist-5; Depression Anxiety Stress Scale</li> <li>Main findings:</li> </ol>
Raffard et al., 2022	Cross-sectional study $N=100 \ patients \ with \ SZ \ and \ 72 \ non-clinical \ controls$ From 4 independent sites in France	Heterosexual orientation, black race, non-Hispanic white, lower education, lower income,     Republican, Independent and other political preference as opposed to Democrats     Lifetime trauma exposure, PTSD symptom severity were not associated with vaccine hesitancy versus acceptance     Outcome measures: PANSS; Green Paranoid Thoughts Scale; Vaccination Attitudes Examination Scale     Main findings:
Vallecillo et al., 2022	$\label{eq:cross-sectional} Cross-sectional study $N=362$ individuals with Opioid Use Disorder from public addiction treatment centres in Barcelona, Spain $$(N=1)$ and $(N=1)$ are considered as $(N=1)$ and $(N=1)$ are considered as $(N=1)$ and $(N=1)$ are considered as $(N=1)$$	<ol> <li>Higher levels of negative psychotic symptoms and higher levels of paranoid ideation (lack of trust in institutions)</li> <li>Outcome measures: Rate of vaccination coverage (number of patients who received vaccination divided by the total number of patients who were offered the vaccination).</li> <li>Main findings:</li> </ol>
Nguyen et al., 2022	Cross-sectional study  N = 5551 individuals from US general population, of which  1 in 3 identified having anxiety or/and depression	1. Education 2. Complacency, convenience and lack of confidence in healthcare workers and vaccine safety -significant barrier to vaccination 3.Brief counseling increased odds of vaccination (76% received both doses of vaccines as a result) Outcome measures: The Household Pulse Survey (HPS); items from the Patient Health Questionnaire (PHQ-2) and Generalized Anxiety Disorder (GAD-2) Scale  Main findings: 2. Adults with anxiety and depression were less likely to receive vaccination than those without; mental health symptoms were less likely to receive vaccination; concerns about possible vaccine side effects, efficacy, cost, dislike or vaccines, lack of trust in the government and vaccines.

literature related to Covid-19 on the topic selected that was published in English between January 2020 and August 20, 2022.

After excluding duplicates, 207 articles were screened by title and abstract in order to identify the ones focusing on explicit factors identified as possible determinants in vaccine hesitancy and acceptance of the vaccination in a psychiatric population. Psychiatric disorders considered for the selection were: anxiety, depression, schizophrenia, and substance use disorders. A total of 135 records were excluded if they did not specifically include participants with a psychiatric condition. The remainder of 72 records were assessed by reading the full-text, which further led to the exclusion of 57 articles if they did not identify factors that could contribute to vaccine hesitancy. For this scoping review we included 15 articles describing results of assessments of factors contributing to vaccine uptake and vaccine hesitancy in a psychiatric population in the context of the Covid-19 pandemic – as seen in the diagram below (Fig. 1. Flow chart diagram of search strategy).

# 3. Results

Our results are summarized in Table 1. (Study population characteristics, outcome measures and main findings in the selected studies).

Table 1 includes the 15 articles selected for this review's purpose (main author, year of publication and journal) as well as the type of study, sample size, target population, outcome measures and main findings including risk factors for Covid 19 vaccine hesitancy (diagnosis, age, gender, smoking, living situation, income, educational level, etc.)

# 4. Discussion

# 4.1. Common findings

One of the most common findings in the studies considered for this review, is that patients with mental illnesses typically had lower vaccination rates or more vaccination hesitancy (Eyllon et al., 2022; Huang et al., 2021; Jefsen et al., 2021; Bai et al., 2021; Perlis et al., 2022; Hao et al., 2021) confirming a numerous studies suggesting this (Wang et al., 2021). Specifically, individuals with severe mental illness, including schizophrenia, were least likely to accept vaccination (Huang et al., 2021; Bai et al., 2021; Tzur Bitan et al., 2021; Raffard et al., 2022). This was often attributed to barriers including mental health and disorder stigma and impaired decision-making skills (Huang et al., 2021; Tzur Bitan et al., 2021). Lower socioeconomic status (SES) was found to be associated with increased likelihood of vaccine resistance (Eyllon et al., 2022; Huang et al., 2021; Tzur Bitan et al., 2021; Nishimi et al., 2022), while having a higher education was associated with less vaccine hesitancy (Eyllon et al., 2022; Huang et al., 2021; Uvais, 2021; Nishimi et al., 2022). It was also found that younger respondents had higher likelihoods of vaccine hesitancy (Eyllon et al., 2022; Jefsen et al., 2021; Tzur Bitan et al., 2021).

Interestingly, it was also found that research participants of African American heritage were associated with increased vaccine hesitancy (Eyllon et al., 2022; Sullivan et al., 2022; Nishimi et al., 2022), as well as those of Hispanic (Eyllon et al., 2022) and Islamic (Uvais, 2021)

backgrounds, which could also be attributed to a lower educational level. Sullivan et al. (2022) attributed the lower willingness to vaccinate seen in Black Americans to possibly greater medical and government mistrust based on present or past discrimination. Only two studies assessed the role of gender in vaccine hesitancy without conclusive results. Being male was identified as a possible vaccination hesitancy factor in one of the studies (Tzur Bitan et al., 2021) while being female was identified in Eyllon et al. (2022).

A few studies found that anxiety disorders and PTSD were significantly associated with vaccine uptake (Huang et al., 2021; Hao et al., 2021, McNeil and Purdon, 2022; Nishimi et al., 2022; Nguyen et al., 2022).

Two studies related to substance use disorders (Vallencillo et al., 2022; Sullivan et al., 2022) found no significant correlation between substance use and vaccine hesitancy but Vallencillo and his team (2022) applied a counseling approach which increased the odds of vaccination.

The common findings of these studies recognize risk factors for Covid 19 hesitancy as: diagnosis of severe mental illness such as schizophrenia (impaired decision making), lower socioeconomic status, lower educational level, and young age. Kumar et al. (2016) found that he main determinants of vaccine hesitancy not related to the Covid-19 are consistently seen as belonging to these 3 categories: environmental, vaccine specific, and host specific and include similar factors: race/ethnicity, educational level, income, knowledge about vaccine and past experiences.

# 4.2. Special findings

In one study which considered different types of psychiatric conditions, it was found that the relationship between vaccine hesitancy and most psychiatric conditions was completely attenuated after regression models for sociodemographic characteristics, except in substance and tobacco use disorders (Eyllon et al., 2022). This was attributed to possible challenges prioritizing healthcare over substance use and medical stigmatization, in addition to poorer compliance with preventative care due to factors including socioeconomic deprivation (Eyllon et al., 2022).

Huang and his team (2021) suggest that other barriers including stigma around mental disorders, priority vaccination controversy, impaired decision-making, and lack of specific clinical guidelines for persons with mental disorders may be possible causes of vaccine hesitancy.

Uvais (2021) made an interesting discovery that participants had significantly higher confidence and preference for locally manufactured vaccines, which may be attributed to India being a major vaccine manufacturer. This may also be attributed to circulating beliefs that Chinese-made COVID-19 vaccines are manufactured with a pork-derived ingredient, which would also help to explain significantly higher vaccine hesitancy in Islamic participants (Uvais, 2021).

Bai's team (2021) found that vaccine hesitancy was more likely in patients in community dwelling compared to hospitalized patients, as a result of less educational support on vaccination.

Perlis et al. (2022) found that presence of depression was significantly associated with increased likelihood of endorsing misinformation, which was associated with decreased likelihood of vaccination willingness. Further, they found that respondents who endorsed at least one misinformation item were significantly less likely to be vaccinated, but also significantly less likely to have a vaccinated family member (Perlis et al., 2022). These findings persisted even after adjustment for sociodemographic features, and self-reported ideology or political party affiliation. These conclusions could be attributed to pronounced negativity bias, or an attentional bias where negative thoughts tend to receive greater focus, in major depressive disorder patients.

One study had significantly different findings from the other papers as it found that the majority of patients suffering from severe mental illnesses were willing to get vaccinated and that willingness to become vaccinated was independent of clinical condition severity (Danenberg

et al., 2021).

Sullivan et al. (2022) found that there were differences in vaccination willingness based on the efficacy of the vaccine, where 20% of participants were unwilling to vaccinate if the vaccine was both safe and highly effective while 68% were unwilling if presented with only a partially effective vaccine. They also found that trust in physicians was positively associated, albeit not significantly correlated, with one's willingness to vaccinate with a partially effective but safe vaccine (Sullivan et al., 2022).

Hao et al. (2021) considered how costs may affect willingness to be vaccinated, and found that more people with depression and anxiety were willing to pay more than \$250 for vaccines, which they found was associated with high DASS-21 (Depression, Anxiety and Stress Scale) scores. This was attributed to these psychiatric conditions having less impact on occupational function, and that there were fewer healthcare workers in the depression and anxiety group. Healthcare occupations were associated with less willingness to pay for vaccination due to possible underpayment of healthcare workers or an expectation of free vaccination. They also noted that internalized stigma was significantly associated with willingness to pay for COVID-19 vaccines in healthy controls, thus suggesting that it acted as a motivator for vaccination (Hao et al., 2021).

Finally, Tzur Bitan et al. (2021) found that schizophrenia patients had sharper declines in survival rates, and milder incline for vaccination as time progressed. They also had higher hospitalization and mortality rates. This study attributed these trends to barriers including accessibility issues, costs, fears, and absence of medical recommendations. They also found that those living in collective facilities were more likely to receive vaccination.

#### 4.3. Limitations

Many studies had low generalizability (Eyllon et al., 2022; Hao et al., 2021; Tzur Bitan et al., 2021), while also presenting selection bias (Eyllon et al., 2022), social desirability bias (Huang et al., 2021; Jefsen et al., 2021; Sullivan et al., 2022), non-response bias (Jefsen et al., 2021), limited minority recruitment (Sullivan et al., 2022; Tzur Bitan et al., 2021), small sample size (Huang et al., 2021; Danenberg et al., 2021; Hao et al., 2021), and recall and reporting bias (Hao et al., 2021). Jefsen et al. also noted that their study was completed before Astrazeneca was found to be associated with blood clots. Although this was studied and considered in regular populations, the lack of information of its effect in mental illness populations should be considered.

These studies looked at different levels of pathology and diagnostic category; not having control, very different outcome measures, no focus on gender diversity and age, some participants coming from an inpatient and some an outpatient setting.

# 4.4. Future directions

Overarching future directions included creating vaccination promotion strategies specific for the psychiatric population (Eyllon et al., 2022, Huang et al., 2021; Uvais, 2021; Bai et al., 2021). Further, some studies considered creating promotion strategies specific to psychiatric patients of various cultures (Sullivan et al., 2022). Multiple studies also pushed for future studies to consider testing their findings in other populations which may have different cultures, ideologies, and healthcare systems (Eyllon et al., 2022; Huang et al., 2021; Jefsen et al., 2021; Sullivan et al., 2022; Tzur Bitan et al., 2021). Finally, multiple studies proposed a need for more transparent communication concerning vaccine efficacy to these populations (Eyllon et al., 2022; Jefsen et al., 2021; Sullivan et al., 2022).

## 5. Conclusion

Fifteen articles out of 219 publications on the topic of Covid 19

vaccine hesitancy met our inclusion criteria for this review. Looking at the main findings we found the following risk factors for Covid 19 vaccine hesitancy: diagnosis of severe mental illness such as schizophrenia (impaired decision making), lower socioeconomic status, lower educational level, and young age. As pathology severity increases, less awareness around the need for vaccination and misinformation endorsement could be considered an important determinant for vaccine hesitancy. The main limitations of our review reside from the limited number of publications focusing on this specific topic, studied population's heterogeneity, and small sample sizes studied. Further limitations refer to a wide diversity of outcome measures used. Also, studies examined different diagnostic categories at different levels of pathology severity, only a few including healthy controls, as well as coming from different settings (inpatients/outpatients). It is possible that the availability of different types of vaccines with different media-promoted side effects may have had an influence on the vaccine hesitancy but none of the discussed studies have mentioned this. Our findings may contribute to the proactive development of educational strategies targeting the psychiatric population tailored to the specific culture, ethnicity, age and gender diversity.

#### Conflict of interest

The authors have no conflict of interest to declare.

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